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10/522,371	01/25/2005	William Richard Cross	15892.9	1386

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EXAMINER	
SCHUBERG, LAURA J	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/522,371	CROSS ET AL.	
	Examiner	Art Unit	
	Laura Schuberg	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/4/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 13-32 are pending and have been examined on the merits.

Response to Arguments

Applicant's arguments filed 06/28/2007 have been fully considered but they are not persuasive. The arguments have been addressed in so far as they relate to the new rejections.

Applicant argues that the Zhang reference does not teach each and every element of the claimed invention. Applicant asserts that Zhang is completely devoid of teaching a "method of production of stratified, differentiated mammalian urothelium in which urothelial cells, isolated from the mammalian body, are passaged through a first nutrient medium containing components of serum and then redispersed before being added to a second medium containing components of serum to form the urothelium" as recited in claim 13.

This is not found persuasive because the method taught by Zhang et al. inherently contains all the claim limitations. To invalidate a patent by anticipation, a prior art reference normally needs to disclose each and every limitation of the claim. See *Standard Havens Prods., Inc. v. Gencor Indus., Inc.*, 953 F.2d 1360, 1369, 21 USPQ2d 1321, 1328 (Fed. Cir. 1991). However, a prior art reference may anticipate when the claim limitation or limitations not expressly found in that reference are nonetheless inherent in it. See *id.* and *Verdegaal Bros., Inc. v. Union Oil Co. of Cal.*, 814 F.2d 628, 630, 2 USPQ2d 1051,1053 (Fed. Cir. 1987). Under the principles of

inherency, if the prior art necessarily functions in accordance with, or includes, the claimed limitations, it anticipates. See *In re King*, 801 F.2d 1324, 1326, 231 USPQ 136, 138 (Fed. Cir. 1986). **Inherency is not necessarily coterminous with the knowledge of those of ordinary skill in the art.** See *Titanium Metals*, 778 F.2d at 780. Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art. See *id.* at 782. However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer. See *id.* at 782 ("Congress has not seen fit to permit the patenting of an old [composition], known to others..., by one who has discovered its...useful properties."); *Verdegaal Bros.*, 814 F.2d at 633.

This court's decision in *Titanium Metals* illustrates these principles. See *Titanium Metals*, 778 F.2d at 775. In *Titanium Metals*, the patent applicants sought a patent for a titanium alloy containing various ranges of nickel, molybdenum, iron, and titanium. The claims also required that the alloy be "characterized by good corrosion resistance in hot brine environments." *Titanium Metals*, 778 F.2d at 776. A prior art reference disclosed a titanium alloy falling within the claimed ranges, but did not disclose any corrosion-resistant properties. This court affirmed a decision of the PTO Board of Appeals finding the claimed invention unpatentable as anticipated. This court concluded that the claimed alloy was not novel, noting, "it is immaterial, on the issue of their novelty, what inherent properties the alloys have or whether these applicants discovered certain inherent properties." *Id.* at 782. This same reasoning holds true when it is not a property, but an ingredient, which is inherently contained in the prior art.

The public remains free to make, use, or sell prior art compositions or processes, regardless of whether or not they understand their complete makeup or the underlying scientific principles which allow them to operate. The doctrine of anticipation by inherency, among other doctrines, enforces that basic principle." See *Atlas Powder Co. v. IRECO Inc.*, 51 USPQ2d 1943 (Fed. Cir. 1999).

Thus, a reference may be anticipatory if it discloses every limitation of the claimed invention either explicitly or inherently. A reference includes an inherent characteristic if that characteristic is the natural result flowing from the reference's explicitly explicated limitations. *Continental Can Co. USA, Inc. v. Monsanto Co.*, 948 F.2d 1264, 1269, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991).

Zhang et al. teach the establishment and expansion of cultures of rat (mammalian) urothelial cells in KSFM that contains components of serum (page 419, materials and methods). Since Applicant has not defined the limitation of "components of serum", it must be given its broadest reasonable interpretation as any element that may be found in serum. Since growth factors, such as EGF, are found in serum (as taught by Baur et al. US 5,968,546, column 5 lines 59-63) and are added to the KSFM media used in Zhang et al. (page 419), nutrient media containing components of serum is inherently taught by Zhang et al. The passaging of cells, as taught by Zhang et al., inherently requires that the cells are trypsinized and redispersed into a second medium that also inherently contains components of serum (growth factors) (page 422, column 2). In addition, the KSFM-CM media used was prepared to contain FBS and therefore also contains components of serum as well (page 422, column 1, 3rd full paragraph and

table 1, media 6). Since Zhang et al. teaches a method that includes all the method steps as claimed by Applicant, Zhang et al. inherently anticipates the claimed invention.

Applicant argues that the Liebert reference is completely devoid of teaching a "method of production of stratified, differentiated mammalian urothelium in which urothelial cells, isolated from the mammalian body, are passaged through a first nutrient medium containing components of serum and then redispersed before being added to a second medium containing components of serum to form the urothelium" as recited in claim 13. Applicant asserts that once the urothelium cells of Liebert are cultured in a media containing serum, such cells are not dispersed into the second media containing serum before differentiation or stratification.

This is not found persuasive because the dispersal of the cells into the second media containing serum before any differentiation or stratification is not recited in the claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). In addition, the method steps of Applicant's invention as it is now claimed (i.e. the passaging of urothelial cells using media containing serum) are explicitly disclosed in Liebert et al. (page 184 column 2, lines 22-32).

Applicant argues that the Scriven reference is completely devoid of teaching a "method of production of stratified, differentiated mammalian urothelium in which urothelial cells, isolated from the mammalian body, are passaged through a first nutrient medium containing components of serum and then redispersed before being added to a second medium containing components of serum to form the urothelium" as recited in

claim 13. Applicant asserts that once the urothelium cells of Scriven are cultured in a media containing serum, such cells are not dispersed into the second media containing serum before differentiation or stratification.

This is not found persuasive because Scriven et al. specifically teaches that the urothelial cells are cultured in media containing serum, resuspended in a minimum volume (of media containing serum) and eventually added to another media containing serum (page 1148, column 1, paragraph 2-3). As long as the cells are in contact with the second serum-containing medium they are deemed to be added together.

Applicant argues that the Seijiro reference is completely devoid of teaching a "method of production of stratified, differentiated mammalian urothelium in which urothelial cells, isolated from the mammalian body, are passaged through a first nutrient medium containing components of serum and then redispersed before being added to a second medium containing components of serum to form the urothelium" as recited in claim 13.

This is not found persuasive because the Seijiro reference is cited as a secondary reference to demonstrate the suitability of adult bovine serum for the culture of animal cells. The primary references of Zhang, Liebert and Scriven are interpreted to teach the method of claim 13 as described above.

Applicant argues that the Judd reference is completely devoid of teaching a "method of production of stratified, differentiated mammalian urothelium in which urothelial cells, isolated from the mammalian body, are passaged through a first nutrient medium containing components of serum and then redispersed before being added to a

second medium containing components of serum to form the urothelium" as recited in claim 13.

This is not found persuasive because the Judd reference is cited as a secondary reference and indicates that MCDB-153 is a suitable alternative for KSFM medium in a defined system for epithelial cell culture (column 5 lines 1-13). The primary references of Zhang and Liebert are interpreted to teach the method of claim 13 as described above.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 27-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. New claims 27 and 28 include wherein the culture and/or urothelium is devoid of feeding layers and devoid of growing the cells on 3T3 cells or with media incubated with 3T3 cells respectively. There is not sufficient support in the disclosure as originally filed for these limitations; thus they are being considered new matter. The disclosure as originally filed only supports culturing the

cells with the media such as MCD-153 or KSFM with or without serum and other additional additives. The disclosure as filed does not mention eliminating feeding layers or co-cultures of any kind let alone 3T3 cells from the claimed method. Any negative limitation or exclusionary proviso must have basis in the original disclosure.

An amendment to the claims or the addition of a new claim must be supported by the description of the invention in the application as filed. In re Wright, 866 F.2d 422, 9 USPQ2d 1649 (Fed. Cir. 1989). Applicant is required to cancel the new matter in the reply to this Office Action.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 24-32 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. Zhang et al. recites the same steps as claimed by Applicant, (establishing a primary culture with serum free media and expanding the cells in serum containing media for subsequent passages without a feeder layer or exposure to 3T3 cells), yet does not describe the exact same results (page 427 column 1). It appears that Applicant's claimed method must be missing an essential method step or component that ensures a stratified, differentiated urothelium. This is further supported by the Southgate reference (IDS reference #7) wherein certain factors and components are taught to greatly affect the final outcome of an urothelial culture (page 586, column 1, 1st paragraph- 2nd paragraph and page 590, column 2, 2nd paragraph). All the

essential method steps and media components required for the end result of a stratified, differentiated urothelium must be included in the claimed method in order to be complete.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 13, 15, 17-19, 21-32 are rejected under 35 U.S.C. 102(b) as being anticipated by Zhang et al (In Vitro Cell. Dev. Biol.-Animal 2001).

Amended claim 13 is now drawn to a method of production of stratified, differentiated mammalian urothelium in which urothelial cells, isolated from the mammalian body, are passaged through a first nutrient medium containing components of serum and then redispersed before being added to a second medium containing components of serum to form the urothelium.

Claim 15 includes wherein the serum is bovine serum.

Claims 17-19 include the concentration range of the components of the serum.

Claim 21 includes wherein the nutrient medium is KSFM.

Amended claim 22 includes wherein the nutrient medium is supplemented by one or more of EGF, BPE, or CT.

Claim 23 is drawn to the urothelium produced by the method of claim 13.

New claim 24 is drawn to a method of production of stratified, differentiated mammalian urothelium comprising: culturing the cells into a first cell culture medium devoid of serum to form a primary culture; dispersing the cells into a second cell culture medium that includes serum; culturing the cells to form a secondary cell culture having aggregated cells; dispersing the aggregated cells into a third cell culture medium that includes serum; and culturing the cells to form a stratified, differentiated mammalian urothelium.

New claims 25 and 26 include wherein the aggregated cells are at least partially confluent and approach confluency respectively.

New claim 27 includes wherein the secondary cell culture and/or urothelium is substantially devoid of a feeding layer of cells.

New claim 28 includes wherein the second or third cell culture medium is substantially devoid of growing the cells on 3T3 cells or with media incubated with 3T3 cells.

New claims 29 and 30 include wherein the serum is between about 1% and 30% and 4% and 6% of the medium respectively.

New claim 31 includes wherein the first, second or third cell culture medium is one of MCDB-153, KSFM, or derived thereof.

New claim 32 includes wherein the first, second or third cell culture medium is supplemented by EGF, BPE, or CT.

Aggregated cells are interpreted to mean at least two or more cells that are touching each other.

Zhang teaches a method for expansion and long-term culture of differentiated normal rat urothelium cells in vitro wherein the urothelium cells are isolated from the mammalian body (page 419 materials and methods) and cultured with a media that contains KSFM and conditioned medium (CM) with 5% fetal bovine serum (FBS) (page 422 table 1, media number 6). Detailed investigations of culture conditions showed that CM-KSFM yielded a differentiated multilayered (stratified) structure (abstract). Establishment of primary cultures with a serum free media that contains EGF, BPE and CT is taught (page 419 materials and methods) along with subsequent expansion with different medias containing serum (one with 5% FBS) until passage 2, which would inherently require a second and third culture medium that includes serum (page 422, column 1, paragraph 3-4). The cells are at least partially confluent and approaching confluency and therefore contain cells that are touching each other (aggregated)(page 427 column 1). The cells in one particular embodiment are devoid of feeder layers and 3T3 cells. Though the final product of the method not using feeder layers or 3T3 cells is not described as stratified and differentiated (page 427), the final product is deemed to be the same as that produced by the claimed method since all the claimed method steps are carried out.

Since Zhang et al. is explicitly carrying out all the method steps as claimed by Applicant, Applicant's method as claimed is anticipated.

Claims 13 and 15, 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Liebert et al (Differentiation 1997).

Liebert teaches a method of producing a stratified urothelium using urothelial cells that were passaged with media containing bovine serum (page 184 column 2 lines 22-32). Since the invention as claimed does not require a specific level of differentiation or stratification, any degree of differentiation or stratification found in the prior art urothelium would meet these limitations.

Therefore, Liebert anticipates the invention as claimed.

Claims 13-15, 17, 18, 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Scriven et al (The Journal of Urology 1997).

Claim 14 includes wherein the urothelium is human urothelium.

Scriven teaches a method of producing urothelium from cells isolated from urothelium tissue that forms a stratified, polarized transitional-like neo-urothelium that expressed many of the phenotypic and differentiated characteristics of normal tissue (page 1151). The method uses a medium supplemented with 10% fetal bovine serum and the cells are passaged and redispersed before going on to be added to a second media containing serum and forming a urothelium (page 1148 materials and methods). As long as the cells are in contact with the second serum-containing medium they are deemed to be added together. Since the invention as claimed does not require a

specific level of differentiation or stratification, any degree of differentiation or stratification found in the prior art urothelium would meet these limitations.

Therefore, Scriven anticipates the invention as claimed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang et al (In Vitro Cell. Dev. Biol.-Animal 2001) or Liebert et al (Differentiation 1997) or Scriven et al (The Journal of Urology 1997) in view of Seijiro et al (US 4,654,304).

Claim 16 is drawn to the method of claim 15 wherein the serum is adult bovine serum.

Zhang, Liebert or Scriven teach the method of claim 15 as described above, but do not include adult bovine specifically.

Seijiro teaches that serum to be used in the cultivation of animal cells or tissues may be derived from any species, although bovine, among others, may be advantageously used for reasons of their ready availability (column 1 lines 64-68). The mammals from which the serum is derived may be at any age, e.g., fetuses, newborns, youngs or adults (column 2 lines 1-2). Clearly adult bovine serum is considered by Seijiro to be a suitable substitute for fetal or newborn bovine serum.

Therefore, one of ordinary skill in the art would have been motivated to substitute adult bovine serum for fetal or newborn bovine serum because Seijiro teaches that mammals from which the serum is derived may be at any age, e.g., fetuses, newborns, youngs or adults (column 2 lines 1-2). One of ordinary skill in the art would have had a reasonable expectation of success because Seijiro had demonstrated that the adult bovine serum possessed growth promoting substances (column 11 table 4).

Therefore, the combined teachings of Seijiro with any one of Zhang, Liebert or Scriven render obvious the invention as claimed.

Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Zhang et al (In Vitro Cell. Dev. Biol.-Animal 2001) in view of Judd et al (US 6,692,961 B1).

Claim 20 includes wherein the nutrient medium is, or is a derivative of, MCDB-153 medium.

Zhang teaches the method of claim 13 using KSFM, but does not teach the use of MCDB-153 medium.

Judd teaches a defined system for epithelial cell culture and indicates that MCDB-153 is a suitable alternative for KSFM medium (column 5 lines 1-13).

Therefore, one of ordinary skill in the art would have been motivated to substitute MCDB-153 medium for KSFM in the method of Zhang because Judd indicates that MCDB-153 is a suitable alternative for KSFM medium (column 5 lines 1-13). One of ordinary skill in the art would have had a reasonable expectation of success because the teachings of Judd were drawn to the in vitro cultivation of animal epithelial cells.

Therefore, the combined teachings of Zhang and Judd render obvious the invention as claimed.

Claims 20 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Liebert et al (Differentiation 1997) in view of Judd et al (US 6,692,961 B1).

Liebert teaches the method of claim 13 as described above, but does not teach the use of MCDB-153 medium or supplementing with EGF, BPE, CT.

Judd teaches a defined system for epithelial cell culture and indicates that MCDB-153 (which includes EGF and BPE) is a suitable alternative for KSFM medium (column 5 lines 1-13). Judd also teaches the benefits of adding EGF and/or cholera toxin (CT) to the media as well (column 11 lines 10-40).

Therefore, one of ordinary skill in the art would have been motivated to use MCDB-153 in the method of Liebert because Judd teaches that MCDB-153 is a suitable alternative for the media that Liebert uses (KSFM). One of ordinary skill in the art would have been motivated to add EGF or CT to the culture media of Liebert because Judd teaches that these agents are beneficial in the growth of epithelial cells. One of ordinary skill in the art would have had a reasonable expectation of success because both Judd and Liebert are growing epithelial cell cultures.

Therefore, the combined teachings of Liebert and Judd render obvious the invention as claimed.

Claims 13-15, 17-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cross et al. (Biochemical Society Transactions 2001, from IDS) in view of Zhang et al (In Vitro Cell. Dev. Biol.-Animal 2001).

Cross et al. teach that normal human urothelial cells propagated in serum-free medium exhibited a low transepithelial electrical resistance and a high FITC-Dextran permeability. The addition of serum to the culture system resulted in urothelial stratification, intercellular tight junction formation, a high transepithelial electrical resistance, a low FITC-Dextran permeability and the expression of amiloride sensitive sodium channels. This human *in vitro* urothelial tissue model expresses many of the morphological and functional properties of the *in vivo* system (abstract).

Cross et al. are silent with regard to the exact media used and the number of passages from the establishment of primary cultures to the final product.

Zhang et al. teach that KSFM provides an optimal medium to separate urothelial cells selectively from other types of cells and can be used for an initial culture before subculturing (redispersing) the cells in a serum-supplemented media for long-term cultures (page 428, column 1, paragraph 3). Establishment of primary cultures with a serum free media that contains EGF, BPE and CT is taught (page 419 materials and methods) along with subsequent expansion with different medias containing serum (one with 5% FBS) until passage 2, which would inherently require a second and third culture medium that includes serum (page 422, column 1, paragraph 3-4). The cells are at least partially confluent and approaching confluency and therefore contain cells that are touching each other (aggregated) (page 427 column 1).

Therefore, one of ordinary skill in the art would have been motivated to use a serum free media such as KSFM in the establishment of primary urothelial cultures because Zhang et al. teach that KSFM provides an optimal medium to separate urothelial cells selectively from other types of cells and can be used for an initial culture before subculturing (redispersing) the cells. One of ordinary skill in the art would have been motivated to switch to media containing serum for the subsequent passages of urothelial cells because Cross et al. teach that the addition of serum containing media to urothelial cultures yields a human *in vitro* urothelial tissue model expressing many of the morphological and functional properties of the *in vivo* system (abstract). The number of passages required would have been a matter of routine optimization, the artisan of ordinary skill requiring to adjust the number of passages depending on the amount of urothelium required for the end product. One of ordinary skill in the art would have been

motivated to use bovine serum at about 5% and other growth factors such as EGF, BPE and CT because Zhang et al. teach that these are suitable additions and concentrations for the growth of urothelial cells. One of ordinary skill in the art would have had a reasonable expectation of success in using these techniques in the method of Cross et al. because Zhang et al. teach that culture techniques such as these are applicable to other primary tissue culture systems where potential contamination and subsequent overgrowth with fibroblasts remain a problem (page 428, column 2, last paragraph).

Therefore, the combined teachings of Cross et al. and Zhang et al. render obvious Applicant's invention as claimed.

Conclusion

No claims are allowed.

Applicant's amendment and submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on 09/04/2007 prompted the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a) and MPEP § 609.04(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura Schuberg whose telephone number is 571-272-3347. The examiner can normally be reached on Mon-Fri 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Leon B Lankford, Jr
Primary Examiner
Art Unit 1651

Laura Schuberg